

BACKGROUND: Prior Hepatic Immunotherapy for Metastases (HITM) phase I/II studies demonstrated the safety and biologic activity of anti-CEA CAR-T cell hepatic artery infusions (HAI) for CEA liver metastases (LM). Here we report preliminary HITM-SURE data using Pressure-Enabled Drug Delivery (PEDD) technology for HAI to overcome high intra-tumoral pressures.

METHODOLOGY: Candidates had unresectable CEA+ LM and failed >1 line of systemic therapy. Enrolled patients received 3 HAI of 10x10^10 second generation (IgG2B8TCCR) anti-CEA CAR cells (Sorrento Therapeutics) via a PEDD (Surefire Medical) device and low dose IL-2 (50,000 IU/kg/day). Objectives were to evaluate the safety profile of CAR-T HAI with PEDD and to secondarily assess clinical response.

RESULTS: At study conclusion, 4 male and 1 female pts completed treatment—mean age 55.8 yrs (38-64) with 1-6 lines of prior chemotherapy. There was an average of 7.4 LM with an average maximal diameter of 2.8 cm. Mean CAR expression was 68.1% and production time of 11.8 d. In vitro targeted cytotoxicity was 41%. Reduction in serum CEA was observed in all pts during the study period (avg decrease 44%, range 13-67%). Compared to previous HITM CAR-T HAI trials with a standard catheter, PEDD significantly increased the frequency of CAR-T 5.2-fold within LM, as detected by quantitative PCR (p=0.03). No Grade (G) 4 or 5 AEs related to CAR-T HAI vs PEDD were detected. G1/2 events were largely attributed to IL-2 infusion and were comparable to prior HITM studies. One pt experienced grade 3 colitis, which resolved with IL-2 dose reduction and had colon biopsies that were negative for CAR-T by PCR and immunofluorescence. Twelve-month follow-up imaging in one pt with stage IV pancreatic carcinoma revealed no evidence of LM on PET and his primary pancreatic tumor was stable. Serum and LM biopsies from this pt reveal increased expression of IFN-g and IL-6 in LM, with decreased expression of IL-17, PD-L1, IDO and GM-CSF. A second pt with stage IV pancreatic cancer had no evidence of LM on PET at 6 weeks following CAR-T infusions. Mean and median survival times were 9.3 and 7.5 months for all patients, and 10.0 and 8.4 months for subjects with stage IV pancreatic cancer.

CONCLUSION: Early results from the HITM-SURE study indicate that HAI of CAR-T using PEDD is well tolerated and results in encouraging activity against CEA+ LM. The median OS compares favorably with prior HITM studies and presently approved second/third line regimens. Final results will inform design and device choice for larger studies. NCT02850536